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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/468,145	06/06/1995	JURGEN ENGEL	Y17506/93-11	4889

7590

01/22/2002

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EXAMINER

MINNIFIELD, NITA M

ART UNIT

PAPER NUMBER

1645

DATE MAILED: 01/22/2002

37

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/468,145

Applicant(s)

ENGEL ET AL.

Examiner

N. M. Minnifield

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 October 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 20-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 20-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment filed October 11, 2001 is acknowledged and has been entered. Claims 9 and 10 have been cancelled. Claims 20-23 are now pending in the present application. It is noted that prosecution has been re-opened in this application and that a new grounds of rejection has been set forth. The Examiner regrets any inconvenience.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. Claims 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolf et al (DD 411996) taken with Behre et al (1992), Reissmann et al (1994) and Diedrich et al (1994).

The claims are directed to a method for the preparation of a sterile Cetrorelix lyophilizate, said method comprising the steps of dissolving the Cetrorelix in aqueous acetic acid to form a solution, diluting the solution with water, adding a bulking agent (hexitol, mannitol, etc), sterile filtering, dispensing into injection vials and lyophilizing the solution, thereby obtaining a sterile Cetrorelix lyophilizate.

Wolf et al teach methods of preparing lyophilized synthetic LHRH, which preparation is stable at room temperature over a long period of time (page 1 of English translation; p. 3-4). Wolf et al teach the use of vehicle (i.e. mannitol; bulking agent) and buffer (i.e. acetic acid) substance for the adjustment of an

optimal range of the hydrogen-ion concentration, pH (p. 2; p. 4). The prior art teaches that the application can be for veterinary medicine as an estrus-synchronization agent as well as *inter alia* in the human medicine as an agent in the case of treating fertilization disorders (p. 2-3). Wolf et al teach sterilization by filtration and that the solution is lyophilized (p. 5). The prior art teaches the claimed invention except for the specific preparation of Cetorelix lyophilizate.

However, Behre et al teach that GnRH antagonist Cetorelix (an antagonistic analog of GnRH) has the potential for treatment of sex hormone-dependent diseases and male contraception (abstract). Behre et al teach the use of Cetorelix in lyophilized for injection and was dissolved in water containing mannitol (p. 394). Reissmann et al (1994) teach that Cetorelix is a LHRH antagonist and that the "release of the gonadotrophins, luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the pituitary gland is regulated by a peptide hormone named luteinizing hormone releasing hormone (LHRH)." (p. 767). Reissmann et al teach the need for synthesizing antagonists of LHRH and that Cetorelix is one of the most advanced, being used in a variety of animal models as well as in clinical studies including normal young men and women (p. 767). Cetorelix has been tested in combination with human menopausal gonadotrophin (HMG) for ovarian stimulation in in-vitro fertilization regimens, comprising the first introduction of an LHRH-antagonist in the indication (p.767). Cetorelix has been administered by daily s.c. injections (p. 768). Diedrich et al (1994) teach that Cetorelix is a GnRH antagonist and can be used in the treatment for ovarian stimulation (p. 788). The cetorelix was given by injection (p.789).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use a drug or compound similar to LHRH/GnRH to treat infertility in humans or veterinary medicine. The art teaches the method of preparing the LHRH, which is similar to the Cetorelix, an antagonistic analog of LHRH/GnRH. The Cetorelix is a small peptide similar to LHRH and Wolf et al teaches the same method in preparing the sterile LHRH lyophilizate as claimed by Applicants, using the bulking agent (mannitol), a buffer (acetic acid) and sterile filtering, and lyophilizing the solution. Both the prior art (in combination) and the claimed invention prepare the cetorelix (sterile and lyophilized) for the same purpose and in the same manner. The claimed invention is prima facie obvious in view of the prior art, absent any convincing evidence to the contrary.

4. No claims are allowed.
5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.
6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 703-305-3394. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is

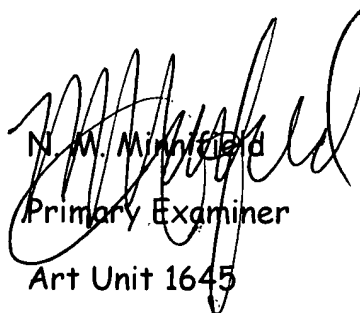
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assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.


N. W. Minnifield
Primary Examiner
Art Unit 1645

January 14, 2002